UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,957	07/28/2003	Marc R. Montminy	088802-2758	6172

30542 7590 03/08/2005

FOLEY & LARDNER
P.O. BOX 80278
SAN DIEGO, CA 92138-0278

EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/628,957	MONTMINY, MARC R.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 6-10* is/are pending in the application.

4a) Of the above claim(s) *9 and 10* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 6-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 1-4, and 6-10 are pending in the application. In the prior action, mailed on November 16, 2004, claims 1-8 were under consideration and rejected, and claims 9 and 10 were withdrawn as to non-elected inventions. In the Response filed on February 15, 2005, the Applicant amended claims 1, 3, 4, and 6-8, and cancelled claim 5.

2. Claims 1-4, and 6-8 are under consideration. Claims 9 and 10 stand withdrawn as to non-elected inventions.

Sequence Listing

3. **(Prior Objection- Maintained)** The Sequence Listing of the present application is objected to for the following reasons: SEQ ID NO: 2 is asserted to be a protein sequence of the CREB Binding Protein (CBP) encoded by SEQ ID NO: 1. The Applicants have attempted to overcome this objection by requesting, in the remarks of the Response, that the sequence listing, both paper and CRF, of the parent application be transferred to the present application.

It is first noted that, although the rules permit the Applicant to use the computer readable form of the sequence listing of a parent application in a later filed application, there is no such provision for the paper copy of the sequence listing. Thus, the Applicant's response is not sufficient to overcome the objection.

Additionally, while the Applicant may use the computer readable form of a parent application in a later filed application, the request to do so must 1) identify the parent application by application number and the CRF as the only filed CRF, or identify the CRF as the first, second, etc., to be filed in the parent. See MPEP § 2422.05. Additionally, the request must

include a statement that the CRF of the parent application, and the paper copy submitted in the present application are identical. A sample statement which may be modified as appropriate has been provided in the MPEP section noted above.

Because the submission by the Applicant has not properly provided a paper copy of the sequence listing in the present case, or provided a sufficient request for transfer of a previously submitted CRF from a parent case, the Applicant's arguments in traversal are not found persuasive. For these reasons, and the reasons of record, the objection is maintained.

Claim Objections

4. **(Prior Objection- Withdrawn)** Claims 7 and 8 were objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. In view of the amendment of the claims such that they are no longer improperly dependent on claim 1, the objection is withdrawn.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. **(Prior Rejection- Maintained)** Claims 7 and 8 were rejected under 35 U.S.C. 101 because the disclosed invention is inoperative and therefore lacks utility. The claims were rejected as reading on inoperable inventions. In particular, the art cited in the prior action indicates that the arginine of position 600 is critical for CBP binding to CREB.

The Applicant traverses the rejection on the basis that they have asserted a utility, and that the fragments are therefore operative. However, the Applicant has provided no evidence that the peptide is in fact able to perform the asserted utility. The unsupported assertion of utility is insufficient to overcome the evidence of inoperability noted in the prior action. In view of the teachings of the art indicating inoperability of the claimed invention, and the lack of evidence to the contrary, the rejection is maintained.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. **(Prior Rejection- Maintained)** Claims 1-8 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claims were rejected based on the inconsistency between the teachings of the art (including a parent patent) and the application with reference to the sequence of SEQ ID NO: 2. The Applicant argues that the incorporation of the sequence listings from the parent application has overcome the rejection. However, in view of the insufficiency of the Applicant's submissions with respect to such incorporation, the argument is not found persuasive. See, above. The rejection is therefore maintained.

For the purposes of this action, unless otherwise stated, reference to SEQ ID NO: 2 is read as reference to the SEQ ID NO: 2 disclosed in the parent application 09/686,316, now U.S. patent 6,646,115.

9. **(Prior Rejection- Withdrawn)** Claims 1, 2, 6-8 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the Applicant's assertion that the fragment is required to bind CREB, and their arguments presented in traversal of the rejection, the rejection is withdrawn.

10. **(Prior Rejection- Maintained)** Claim 6 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it was unclear what is meant by the phrase "mutant fragment." The Applicant traverses the rejection on the grounds that the phrase embraces fragments that "have an alteration is sequence." While this much is clear, it is not clear if the claim is intended to read on such mutant fragments which include alterations in the "all or a portion of CBP which binds to CREB," or if the alterations are outside of such a region (i.e., the fragment comprises the binding region, and additional CBP portions which have been altered). Because the claim is not clear on this point, the rejection is maintained.

11. **(Prior Rejection- Maintained)** Claims 2, 7, and 8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the amendment of claims 7 and 8 to require the presence of residues 461-661 of SEQ ID NO: 2 (wherein residue 600 has been substituted), the rejection is withdrawn from this claim. However, the rejection is maintained with respect to claim 2. The Applicant alleges that the claim amendments have overcome the rejection. It is not clear that this is the case. Claim 2, due to the amendments of

claim 1, read on a nucleic acid encoding a fragment of a CBP which binds to CREB, and which comprises residues 634-648 of SEQ ID NO: 2, and which comprises "the arginine at position 600 of SEQ ID NO: 2." As indicated in the prior action, it is not clear if this additional limitation requires the fragment of claim 2 read on any fragment of any CBP with a residue corresponding to the arginine at position 600 of SEQ ID NO: 2, or is intended to read on only fragments of SEQ ID NO: 2 which comprise this residue. The amendment of claim 1, to require the presence of residues 634-648 of SEQ ID NO: 2, does not clarify the issue because this portion of CBP is common to both the human and the murine CBP. See, Giles et al. (Genomics 42: 96-114- cited in the prior action). However, these two versions of CBP differ in their placement of the arginine corresponding to residue 600 of SEQ ID NO: 2. Because it is not clear if claim 2 is limited to fragments of SEQ ID NO: 2 comprising the arginine of residue 600, or if the claim reads on any fragment of any CBP comprising the residue corresponding to this residue, the rejection is maintained.

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. **(Prior Rejection- Maintained)** Claims 1, 2, 5-8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims were rejected as reading on any nucleic acid encoding any fragment of CBP that binds to CREB. The Applicant has not provided sufficient descriptive support for the claimed genus. The claims (with

the exception of claim 5 which has been cancelled) have now been amended to require that the sequence encodes at least residues 634-648 of SEQ ID NO: 2. The Applicant appears to argue in the Response that this amendment provides a structural feature that correlates with the indicated function, and that the application provides adequate support for such embodiments. The argument is not found persuasive.

While the Applicant has demonstrated that an antibody directed against region of residues 634-648 of SEQ ID NO: 2 inhibited CBP-CREB binding, and therefore that this region is involved in such binding, the application has not established that this region is itself sufficient to permit such binding. I.e., there is no evidence that a peptide consisting if this region would be capable of binding to CREB without additional structural elements from full-length CBP. This is because, as indicated in the prior action, the art teaches that additional elements found outside this region have been found to be critical for CBP/CREB binding. See e.g., Parker et al., Molec Cell Biol, 16: 694-703, at 701. Thus, while the Applicant has provided both a structural feature and a functional feature for the claimed genus of inventions, the identified structural feature has not been demonstrated to correlate to the function.

As noted in the prior action, the Eli Lilly court stated that a functionally defined genus of inventions may be identified by "disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure." Eli Lilly, 43 USPQ2d at 1406. In the present case, the Applicant has merely provided a functional and a structural feature of the claimed genus of inventions, but has not demonstrated that the indicated structure correlates to the presence of the required function. For these reasons, and because there is insufficient

information in the application to demonstrate possession of the genus comprising any fragment comprising this region that binds to CREB (as described in the prior action), the rejection is maintained.

14. **(Prior Rejection- Maintained)** Claims 1, 2, and 5-8 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims were rejected because the Applicant has not provided sufficient information to enable those in the art to make or use any fragment or mutant of CBP wherein the fragments or mutants are able to bind CREB, and therefore nucleic acids encoding them, without under experimentation. The rejection is withdrawn from claim 5, which has been cancelled from the application; and from claims 7 and 8, which no longer contain the functional language. The remaining claims have been amended to require that the claimed nucleic acids encode fragment of CBP which comprises residues 634-648 of SEQ ID NO: 2.

The Applicant traverses the rejection on the basis that the claims have been amended to require the presence of the indicated region of SEQ ID NO: 2, that the application provides some teachings relating to portions of CBP that are involved in the binding to CREB (e.g., residue 600, and the KIX domain). Further, the Applicant also alleges that the art is not unpredictable. This argument is not found persuasive because, although Bowie does indicate that proteins are generally tolerant to substitutions, the reference also teaches that effects of any particular mutation to a protein sequence are not predictable absent teachings relating to the relationship of the mutated residues with the protein's structure and function. While the present application provides certain teachings relating to whether certain regions or residues are involved in CBP's

CREB binding activity, the application has not disclosed any fragments of the protein, other than that of residues 461-661, that are able to bind to CREB. While the application has disclosed certain residues that may are involved in such binding, the application does not teach which portions of the protein are required for such binding, or which residues may be deleted or substituted without abrogating the protein's ability to bind to CREB.

Further, while the application and the art indicate that certain of these residues are required for activity, the claims appear to read on embodiments lacking these residues. For example, claim 2 further limits the inventions to claim 1 to embodiments wherein the fragment comprises the arginine residue at position 600of SEQ ID NO: 2. Thus, under the doctrine of claim differentiation, claim 1 has been indicated to read on embodiments lacking this residue. The claims therefore read on any fragment lacking such a residue although the application teaches its involvement in the binding to CREB, and provides no evidence that proteins lacking this residue would be capable of such binding.

For these reasons, and absent further teachings, the Applicant has not provided sufficient information to enable those in the art to practice the claimed invention to the full extent as claimed without having to discover for themselves which fragments of mutants have the ability to bind to CREB.

It is noted that the Applicant asserts that other working examples may be identified because "homologous sequence can be readily found in public databases." This argument is not found persuasive because a search for a homologous sequence will not necessarily identify proteins that are able to bind to CREB. Additionally, the Applicant has not identified any such homologous proteins that bind to CREB, or identified any common structures with such proteins

and the protein of SEQ ID NO: 2 that correlate with the ability to bind to CREB. Because no homologous CREB binding proteins have been identified, and no comparison of structures and functions have been provided, this argument is also not found persuasive.

For the reasons above, the initial analysis set forth in the prior action is found proper. The Applicant's arguments to the contrary are not found persuasive for the reasons above. The rejection is therefore maintained.

Claim Rejections - 35 USC § 102

15. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

16. **(Prior Rejection- Maintained)** Claims 1 and 6 were rejected under 35 U.S.C. 102(a) as being anticipated by Chrivia et al. (Nature 365: 855-59). The Applicant traverses the rejection on the basis that the claims read on a nucleic acid encoding a fragment of CBP comprising residues 634-648 of SEQ ID NO: 2. The Applicant asserts that the reference does not teach such a nucleic acid. The argument is not found persuasive. As noted in the prior action, the reference teaches a nucleic acid encoding a fusion protein of a CREB binding portion of CBP and a marker polypeptide. Pages 857-58, and Figure 3. The reference teaches that this fragment comprises residues 117-661, or 1-661 of the CBP described in Figure 1 of the reference. This region comprises a sequence corresponding to residues 634-648 of SEQ ID NO: 2. See, protein residues

634-648 of Figure 1. Because these residues are identical to those of residues 634-648 of SEQ ID NO: 2, the Applicant's argument is not found persuasive. The rejection is therefore maintained.

17. **(Prior Rejection- Withdrawn)** Claims 7 and 8 were rejected under 35 U.S.C. 102(b) as being anticipated by Parker et al. (Molec Cell Biol 16: 694-703). These claims read on nucleic acids encoding fragments of CBP including a portion of the region that binds to CREB, and wherein the fragment includes an amino acid corresponding to residue 600 of SEQ ID NO: 2 of the 548 patent, but wherein that residue is a glutamine. They have been amended to require that the nucleic acids encode residues 461-664 of SEQ ID NO: 2 wherein residue 600 is substituted with a an amino acid other than arginine. Because the reference does not teach the making of such a nucleic acid, the rejection is withdrawn.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. **(Prior Rejection- Maintained)** Claims 2-5 and 7 were rejected under 35 U.S.C. 102(a) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Chrivia. These claims previously described the claimed nucleic acid with reference to the sequence of SEQ ID NO: 2, which is disclosed as a murine CBP. The Applicant argues that the reference does not

provide motivation to choose a fragment comprising residues 634-648 of SEQ ID NO: 2. This argument is not found persuasive. The reference suggests the use of a fragment of the CBP comprising at least residues 462-661 of CBP because this domain is disclosed as the CREB binding domain. Additionally, the reference teaches the making of a nucleic acid encoding residues 1-661 of the sequence. Page 858, description for Figure 3. Because such sequences would inherently possess the appropriate residues 634-648, and because, based on the teachings of the reference as indicated above, both the human and murine proteins comprising residues 634-648 of SEQ ID NO: 2, the fragments suggested by the reference would inherently possess the required sequence. It is noted that the term "comprising" is open language, and reads on any fragment within which the sequence of residues 634-648 may be found. The claims are not limited to fragments "consisting of" residues 634-648. For these reasons, and the reasons of record, the rejection is maintained.

Conclusion

20. No claims are allowed.

21. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 3/7/05
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600